Centro di Riferimento per l'Epidemiologia e la Prevenzione Oncologica in Piemonte

AZIENDA OSPEDALIERO - UNIVERSITARIA
Città della Salute e della Scienza di Torino

REGIONE PIEMONTE

S.S. FORMAZIONE PERMANENTE E AGGIORNAMENTO

Evento Formativo Residenziale

**PROGRAMMA REGIONALE DI SCREENING PER IL TUMORE DELLA MAMMELLA**

**PREVENZIONE SERENA – WORKSHOP 2017**

# UN KEY ARTICLE PER UN ANATOMOPATOLOGO


Fondazione del Piemonte per l'Oncologia

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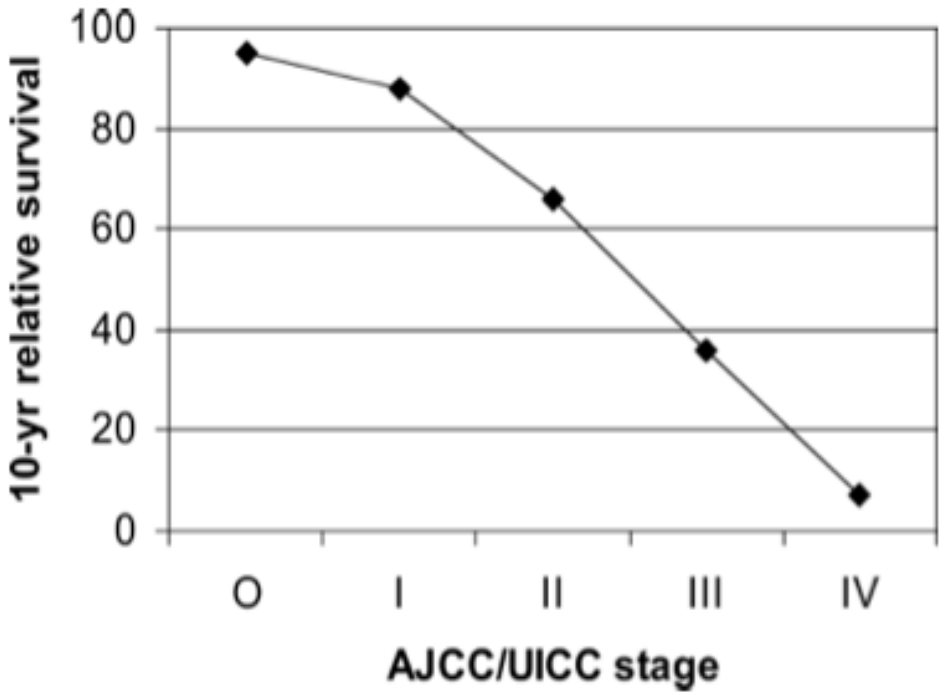
FONDAZIONE PIEMONTESE PER LA RICERCA SUL CANCRO ONLUS


# pTNM staging

IL RUOLO PIÙ IMPORTANTE DEL SISTEMA DI **STAGING**:

**Raggruppare le pazienti in categorie prognostiche, per impostare le terapie adiuvanti**

CA Cancer J Clin 2006;56:37–47




Union for International Cancer Control
**(UICC)**

Gennaio 2017

**POCHI CAMBIAMENTI**

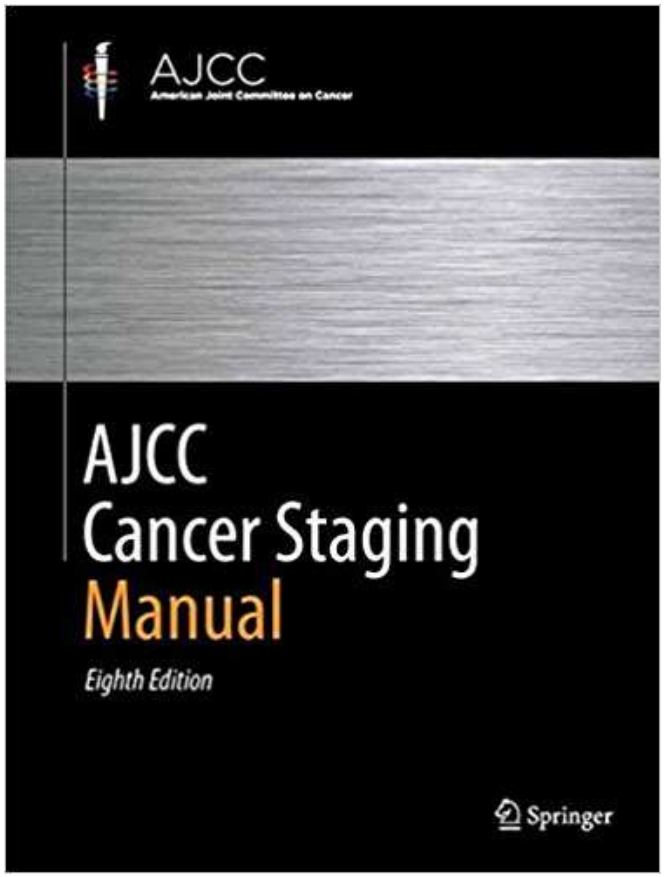
American Joint Committee on Cancer
**(AJCC)**

Gennaio 2018

**MOLTI CAMBIAMENTI**

# Breast Cancer—Major Changes in the American Joint Committee on Cancer Eighth Edition Cancer Staging Manual

Giuliano A et al. CA CANCER J CLIN 2017;67:290–303




## Practical Implications for Continuing Education

- Immunohistochemically detected tumor markers that are known to have great practical treatment importance are now incorporated into the staging system to refine prognosis.
- The eighth edition of the staging system also uses genomic assays when available to downstage some estrogen receptor-positive, lymph node-negative tumors.
- Lobular carcinoma in situ is removed from the staging system because it is not a malignancy but a risk factor. It is no longer considered Tis.

# PRINCIPALI AGGIORNAMENTI
# TNM secondo AJCC, VIII edizione

**TUMORE PRIMITIVO (T)**

## CARCINOMA LOBULARE *IN SITU*

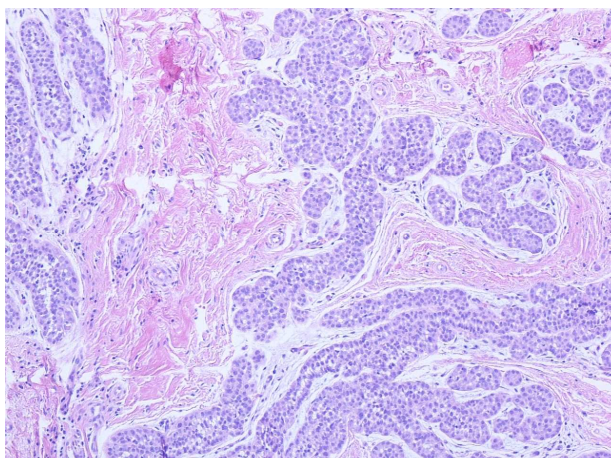
# CARCINOMA LOBULARE *IN SITU* (LCIS)

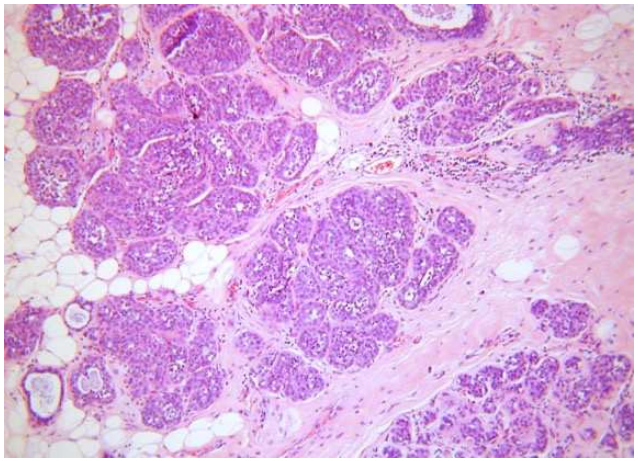
Giuliano A et al. CA CANCER J CLIN 2017;67:290–303

**Rimosso dalla classificazione TNM e dalla categoria patologica T (pTis).**

«LCIS is treated as a **benign entity with an associated risk for developing carcinoma** in the future but not as a malignancy capable of metastases»

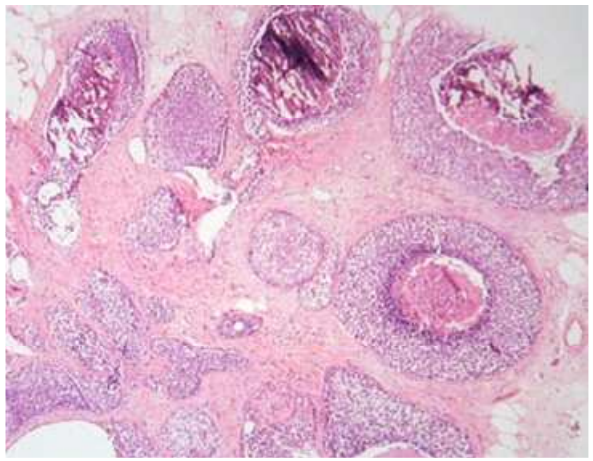
**FOLLOW-UP**





**LIN1/LIN2**

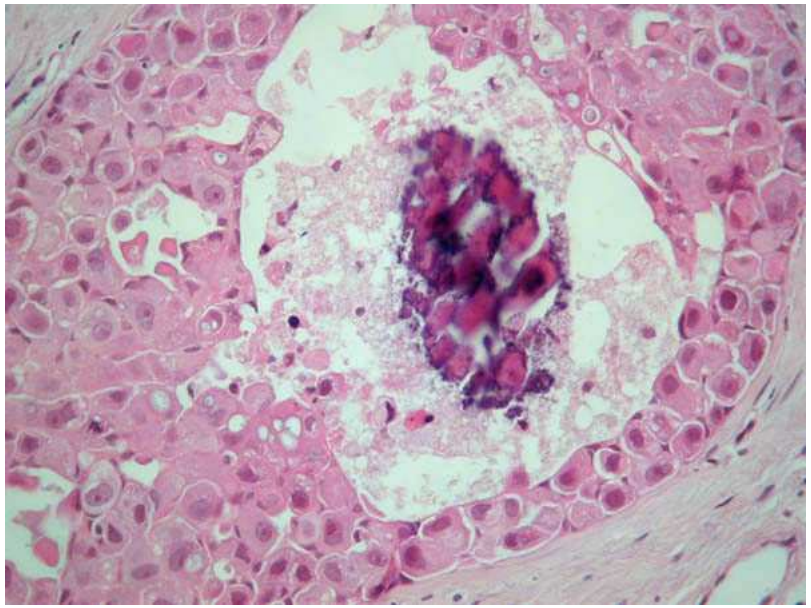
**FOLLOW-UP??**



**LIN3 (PLEOMORFO)**

# CARCINOMA LOBULARE *IN SITU* PLEOMORFO

There is a small subset of LCIS that has high- grade nuclear features and may exhibit central necrosis.



This subset has been referred to as **pleomorphic LCIS** and has histologic features that partially overlap the features of ductal carcinoma *in situ* (DCIS), including the potential to develop calcifications detectable by mammography.

The expert panel debated whether to include this variant of LCIS in the pTis category; however, **there are insufficient data in the literature regarding outcomes and reproducible diagnostic criteria for this LCIS variant**.

**Giuliano A et al. CA CANCER J CLIN 2017;67:290–303**

# PRINCIPALI AGGIORNAMENTI
# TNM secondo AJCC, VIII edizione

**TUMORE PRIMITIVO (T)**

**CARCINOMA LOBULARE *IN SITU***

## VALUTAZIONE DEL DIAMETRO TUMORALE

# VALUTAZIONE DEL DIAMETRO TUMORALE

Giuliano A et al. CA CANCER J CLIN 2017;67:290–303

**1) The size of each macroscopic focus of tumor should be:**

- verified microscopically
- compared with clinical and imaging dimensions

**to assist in establishing the best T classification.**

**2) Microinvasive carcinoma of the breast (pT1mi):**

-tumors measuring < 1.0 mm

-tumors between 1.0 and 1.5 mm should be rounded up to 2.0 mm (pT1a) (Evidence level II)

# PRINCIPALI AGGIORNAMENTI
# TNM secondo AJCC, VIII edizione

**TUMORE PRIMITIVO (T)**

**CARCINOMA LOBULARE *IN SITU***

**VALUTAZIONE DEL DIAMETRO TUMORALE**

## TUMORI SINCRONI

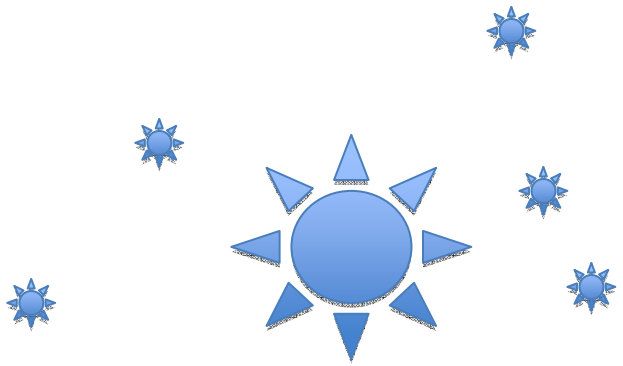
# TUMORI SINCRONI

Giuliano A et al. CA CANCER J CLIN 2017;67:290–303

These are identified clinically and/or by **macroscopic pathologic examination**, and their presence documented using the (**m**) modifier for the T category.

This new edition specifically continues using only the maximum dimension of the largest tumor for clinical (cT) and pathological (pT) T classification; **the size of multiple tumors is not added**.

Generally, incidentally identified **microscopic tumors in proximity to the main tumor mass would be considered SATELLITE FOCI**.



Small, microscopic satellite foci of tumor around the primary tumor do not appreciably alter tumor volume and are **not added to the maximum tumor size**.

# TUMORI SINCRONI

**Giuliano A et al. CA CANCER J CLIN 2017;67:290–303**

Occasionally, **a synchronous invasive tumor** may be **macroscopically missed** in a large excision or mastectomy specimen.

In these situations, **clinical judgment should be exercised, and it would be permissible to use the (m) modifier**, particularly when the tumors have different:

- histology,
- grade, or
- prognostic receptor status.

Each tumor should be tested for ER/PgR/HER2

# PRINCIPALI AGGIORNAMENTI
# TNM secondo AJCC, VIII edizione

**TUMORE PRIMITIVO (T)**

**CARCINOMA LOBULARE *IN SITU***

**VALUTAZIONE DEL DIAMETRO TUMORALE**

**TUMORI SINCRONI**

## TUMORI LOCALMENTE AVANZATI

# TUMORI LOCALMENTE AVANZATI

**Giuliano A et al. CA CANCER J CLIN 2017;67:290–303**

**Satellite tumor nodules in the skin** must be **separate from the primary tumor** and **macroscopically identified** to be classified as **T4b.**

Skin and dermal tumor satellite nodules identified **only on microscopic examination** and in the **absence of skin ulceration or skin edema** (clinical peau d'orange) **do not qualify as T4b**

## pT4d category/inflammatory BC:

- The **erythema/edema** (peau d'orange sign) must be diffuse, **involving at least 1/3 of the breast** (<1/3 pT4b or pT4c)
- the tumour **must have a rapid evolution** with **<6 months** from the first symptoms to the diagnosis of breast carcinoma

(**different from**: **locally advanced BC** producing inflammatory and skin changes in the later course of the disease; not sufficient the presence of lymphatic tumor emboli, which are not need for diagnosis)

# PRINCIPALI AGGIORNAMENTI
# TNM secondo AJCC, VIII edizione

**TUMORE PRIMITIVO (T)**

**CARCINOMA LOBULARE *IN SITU***

**VALUTAZIONE DEL DIAMETRO TUMORALE**

**TUMORI SINCRONI**

**TUMORI LOCALMENTE AVANZATI**

## DOPO TERAPIA NEOADIUVANTE (ypT)

# DOPO TERAPIA NEOADIUVANTE (ypT)

**Giuliano A et al. CA CANCER J CLIN 2017;67:290–303**

When residual tumor is present in the breast, **the largest focus of viable-appearing, residual tumor is used for ypT classification**; treatment-related fibrosis or necrotic-appearing tumor around or adjacent to residual tumor is not included in the maximum dimension.

When **multiple foci of viable residual tumor** are present, the **(m)** modifier should be appended to the ypT classification**.**

When **only residual disease detected is tumor within lymphatic vascular channels (LVI**), although there is **no specific ypT classification** for this situation, and there is no comprehensive outcome analysis for this event, **it would not currently be considered a pathologic complete response.**

# PRINCIPALI AGGIORNAMENTI
# TNM secondo AJCC, VIII edizione

**TUMORE PRIMITIVO (T)**

**CARCINOMA LOBULARE *IN SITU***

**VALUTAZIONE DEL DIAMETRO TUMORALE**

**TUMORI SINCRONI**

**TUMORI LOCALMENTE AVANZATI**

**DOPO TERAPIA NEOADIUVANTE (ypT)**

**LINFONODI (N)**

**ESTENSIONE DELLE METASTASI**

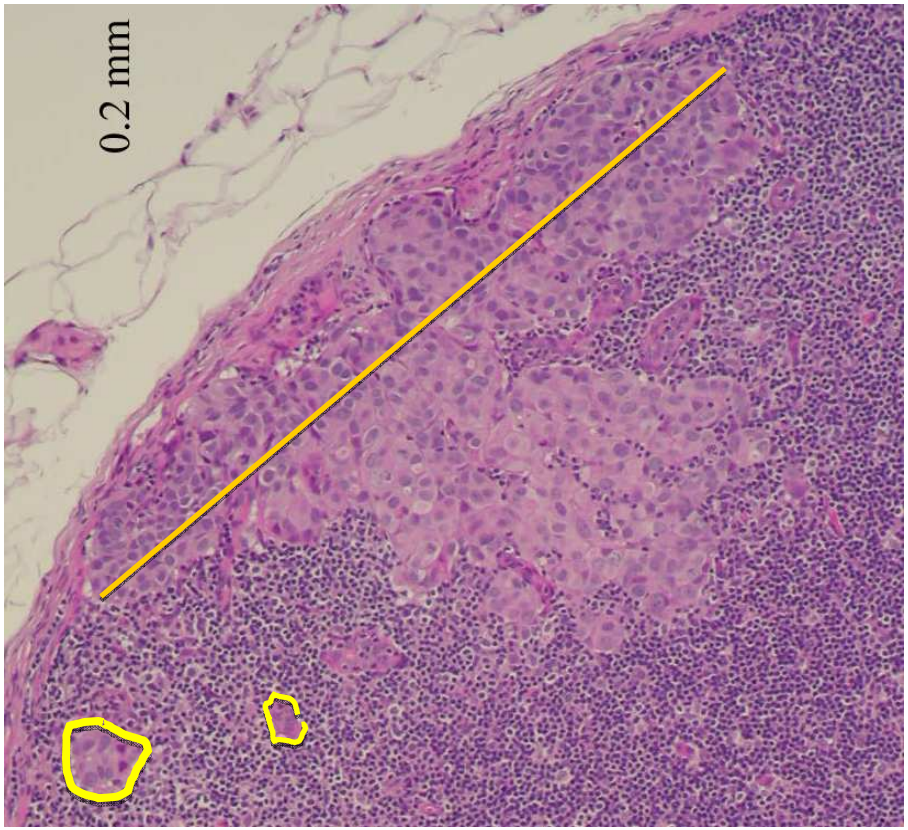
# ESTENSIONE DELLE METASTASI

Giuliano A et al. CA CANCER J CLIN 2017;67:290–303

The expert panel did not recommend **any major changes**

The dimension of the area containing several or multiple tumor deposits is not used to determine the pathologic lymph node (pN) category.

**The largest contiguous tumor deposit is used for pN; adjacent tumor are not added together.**



# ESTENSIONE DELLE METASTASI

Giuliano A et al. CA CANCER J CLIN 2017;67:290–303

## pN(mol)

### PROBLEMS WITH OSNA CLASSIFICATION

It considers the whole tumor burden, thus it may overextimate multiple metastatic foci of different dimensions, since only the largest one should be measured

Qualifiers for either fine needle aspiration cytology or core needle biopsy (f) and sentinel node biopsy (sn) are to be added behind,
to reflect this degree of confidence in nodal staging and to contrast it with staging based on palpation or imaging
[e.g. cN1(f) or cN1(sn) versus cN1].

# PRINCIPALI AGGIORNAMENTI
# TNM secondo AJCC, VIII edizione

**TUMORE PRIMITIVO (T)**

**CARCINOMA LOBULARE *IN SITU***

**VALUTAZIONE DEL DIAMETRO TUMORALE**

**TUMORI SINCRONI**

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**DOPO TERAPIA NEOADIUVANTE (ypT)**

**LINFONODI (N)**

**ESTENSIONE DELLE METASTASI**

**DOPO TERAPIA NEOADIUVANTE (ypN)**

# DOPO TERAPIA NEOADIUVANTE (ypT)

**Giuliano A et al. CA CANCER J CLIN 2017;67:290–303**

Treatment-related fibrosis adjacent to residual lymph node tumor deposits is not included in the ypN dimension and classification.

When residual lymph node disease is present, **the size of the largest focus of residual tumor is used to determine the ypN classification**, and treatment-associated fibrosis is not included, analogous to the ypT classification.

**The pathology report should include a description of the residual tumor in the breast and regional lymph nodes.**

# PRINCIPALI AGGIORNAMENTI
# TNM secondo AJCC, VIII edizione

**TUMORE PRIMITIVO (T)**

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**LINFONODI (N)**

**ESTENSIONE DELLE METASTASI**

**DOPO TERAPIA NEOADIUVANTE (ypN)**

**“FATTORI BIOLOGICI”**
**e**
**TEST MOLECOLARI**

# FATTORI BIOLOGICI E TEST MOLECOLARI

**Giuliano A et al. CA CANCER J CLIN 2017;67:290–303**

*Clinicians often communicate with each other using biologic factors as well as TNM. For example, a colleague might say:*

***"The patient has a T1N0M0, high-grade, triple-negative cancer."***

To address the importance of tumor biology, in addition to defining AJCC anatomic stage groups, the breast **expert panel has defined biologic factor-based prognostic stage groups** for the eighth edition that take into consideration:

**-tumor grade;**

**-HER2, ER, and PR status;**

**-multigene panel (such as Oncotype DX) status**.

# FATTORI BIOLOGICI E TEST MOLECOLARI

**Giuliano A et al. CA CANCER J CLIN 2017;67:290–303**

Although the expert panel **does not endorse any particular assay**, the multigene panel used in the majority of these studies was the 21-gene **Oncotype DX** recurrence score, whereas one study used the 70-gene MammaPrint in conjunction with Adjuvant! Online.

It should be noted that **Oncotype DX is the only multi- gene panel included in the prognostic stage group table of the eighth edition**, because it is supported by level 1 data.

**As of this time, no upstaging is recommended based on multigene panel testing**

A multigene panels would be incorporated into the staging **system only for selected subsets of breast cancer** (eg, hormone receptor-positive, HER2-negative, tone-half, lymph node-negative).

Multigene panels currently in clinical use may simply represent **a substitute for measuring proliferation (???)**.

# FATTORI BIOLOGICI E TEST MOLECOLARI

**Giuliano A et al. CA CANCER J CLIN 2017;67:290–303**

| pT | pN | pM | G | HER2 | ER | PR | 7° | 8° |
|---|---|---|---|---|---|---|---|---|
| **Biomarkers** | | | | | | | | |
| 1 | 0 | 0 | 1 | - | - | - | IA | IIA |
| 1 | 0 | 0 | 3 | - | + | - | IA | IIA |
| 3 | 1-2 | 0 | 1 | + | + | + | IIIA | IB |
| **Oncotype DX <11 for ER+** | | | | | | | | |
| 2 | 0 | 0 | any | - | **+** | any | IIA | IB |
| 1-2 | 1 | 0 | any | - | **+** | any | IIA/IIB | IB |
| 0-2 | 2 | 0 | 1-2 | + | **+** | + | IIIA | IB |

# CONCLUSIONI

It is anticipated that **future modifications** based on biology will undoubtedly be needed with the reporting of additional outcome studies with different panels and longer follow-up, particularly as prospectively designed studies mature.

**DISCUSSIONE MULTIDISCIPLINARE PER STABILIRE DELLE**

**«LINEE GUIDA DI UTILIZZO»**

**DEL TNM 2016 sec. AJCC**

**Meglio se concordate a livello REGIONALE (e poi nazionale)**

# GRAZIE